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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/501,354	12/27/2004	Justin St. John	LA-7492-102	7592

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EXAMINER	
CROUCH, DEBORAH	
ART UNIT	**PAPER NUMBER**
1632	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/20/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/501,354	ST. JOHN ET AL.	
	Examiner	Art Unit	
	Deborah Crouch, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5 and 8-25* is/are pending in the application.

4a) Of the above claim(s) *8-18,20,21,23 and 25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,19,22 and 24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Applicant's election of Group I, claims 1-7 and 19, in the reply filed on February 26, 2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). However, the examiner notes an error in the restriction/election requirement mailed January 30, 2007. The corrected groupings are:

I. Claims 1-5, 19, 22 and 24.

II. Claims 8-13.

III. Claims 14-18, 20 and 23

IV. Claims 21 and 25

As applicant election group I, claims 1-5, 19, 22 and 24 are examined herein.

The information disclosure statement filed July 13, 2004 fails to comply with 37 CFR 1.98(a)(1), which requires the following: (1) a list of all patents, publications, applications, or other information submitted for consideration by the Office; (2) U.S. patents and U.S. patent application publications listed in a section separately from citations of other documents; (3) the application number of the application in which the information disclosure statement is being submitted on each page of the list; (4) a column that provides a blank space next to each document to be considered, for the examiner's initials; and (5) a heading that clearly indicates that the list is an information disclosure statement. The information disclosure statement has been placed in the application file, but the information referred to therein has not been considered.

Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the

requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609.05(a).

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 24 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claim 24 states "an animal," which encompasses humans. This subject matter precluded by the PTO policy (1077 O.G. 24 April 21, 1987). This rejection can be overcome by inserting "nonhuman" before animal.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, 19, 22 and 24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of production a viable hybrid *mammalian* cell having a single functional mitochondria population comprising the step of introducing genomic DNA from a mitochondrially depleted mammalian donor cell in to a reciepient mammalian cell of the same species from which genomic DNA has been removed, does not reasonably provide enablement for the method for any cell or transpecies mitochondria. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification and the art only provide guidance for the depletion of mitochondria from mammalian cells. Guidance is not provided on depletion of mitochondria from species such as insects, amphibians, birds, or plants to name a few. Meirelles demonstrates that methods of nuclear transfer where the nuclear material of *Bos indicus* is inserted into the oocyte of *Bos taurus* produces calves comprising the nuclear material of *Bos indicus* and the mitochondria of *Bos taurus*. Meirelles *et al.* teach that previous attempts to use the *Bos* oocyte as hosts for nuclear transfer from unrelated species allowed development to the blastocyst stage, and conclude that incompatibility among the nuclear and mitochondrial genetic systems is responsible for the early arrest. Meirelles *et al.* also point to similar failures using *Mus caroli* and *Mus musculus* citing Dominko *et al.* Meirelles *et al.* conclude that in light of their results and the failures of the prior art, that nuclear transfer across subspecies barriers is possible. (see Meirelles, pp. 351-355). As the disclosed use of the method is for nuclear transfer to produce identical offspring, there must be a reasonable correlation between the disclosure and the claims.

Thus at the time of the instant invention, the skilled artisan would have needed to engage in an undue amount of experimentation without a predictable degree of success to implement the invention as claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 22 and 24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 22 is improperly dependent on claim 19, which is to a hybrid cell, and not a method.

Claim 24 likewise refers to the "method of claim 19," but claim 19 is to a hybrid cell.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 19, 22 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Meirelles et al. (2001) Genetics, Vol. 158, pp. 351-356.

Claims 19, 22 and 24 are products produced by a particular process. The products are "old" known in the art at the time of filing. Thus, the products claimed would only be patentable if there was a patentable distinction between them. There is no evidence on the record that cells and animals made by the claimed method have any new property or structure imbued by the method.

Meirelles teaches a Bos indicus calf cloned by transfer of a Bos indicus blastomere into an enucleated Bos taurus oocyte (page 353, col. 1, parag. 1, lines 7-16). The cells of the resulting calf contain only Bos taurus mitochondria (page 354, col. 1, parag. 1, lines 11-18; and Figure 3, lines 11-12).

[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985).

"The Patent Office bears a lesser burden of proof in making out a case of prima facie obviousness for product-by-process claims because of their peculiar nature" than when a

product is claimed in the conventional fashion. In re Fessmann, 489 F.2d 742, 744, 180 USPQ 324, 326 (CCPA 1974). Once the examiner provides a rationale tending to show that the claimed product appears to be the same or similar to that of the prior art, although produced by a different process, the burden shifts to applicant to come forward with evidence establishing an unobvious difference between the claimed product and the prior art product. In re Marosi, 710 F.2d 798, 802, 218 USPQ 289, 292 (Fed. Cir. 1983).

"Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product (*In re Ludtke*). Whether the rejection is based on "inherency" under 35 USC 102, on "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. *In re Best, Bolton, and Shaw*, 195 USPQ 430, 433 (CCPA 1977) citing *In re Brown*, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972))."

"When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the *prima facie* case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. *In re Best*, 562 F.2d at 1255, 195 USPQ at 433. See also *Titanium Metals Corp. v. Banner*, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985), *In re Ludtke*, 441 F.2d 660, 169 USPQ 563 (CCPA 1971), *Northam Warren Corp. v. D. F. Newfield Co.*, 7 F. Supp. 773, 22 USPQ 313 (E.D.N.Y. 1934.) See MPEP 2113 and MPEP 2112.01.

Thus, Meirelles anticipates the claimed invention by teaching cells comprising and a calf whose cells comprise a single mitochondrial population. Alternatively, any differences between the cells and calf of Meirelles and those claimed would be obvious differences that do not affect the structure or use of the cells or calf.

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3 and 5 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Levy et al. (1999) Transgenic Res., Vol. 8, pp. 137-145.

Levy teaches a method of producing homoplasmic mitochondrial hybrid cells or cybrids by enucleating CAP^r 501-1 (HPRT-) cells in the presence of cytochalasin B to produce a cytoplast (page 139, col. 1, parag. 2). Cytochalasin B arrests the ES cells during DNA removal. Levy then electrofuses the enucleated CAP^r cells with AK11.1 ES cells that have been treated with R-6-G, which depletes the cells of functional mitochondria (page 138, col. 2, lines 13-15). The cybrids were cloned in HAT medium (page 139, col. 2, parag. 1). Forty-six out of forty-eight cybrids were homoplastic for the CAP^r mutation (page 143, col. 1, parag. 1, lines 7-8). The cybrids were inherently reactivated after fusion, which introduces the CAP^r cell genomic DNA into the enucleated ES cells, as indicated by cybrid proliferation (page 143, col. 1, parag. 1, lines 8-10). Thus Levy clearly anticipates the claimed invention.

Claims 1, 2, and 4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sims et al. (1993) Proc. Natl. Acad. Sci., Vol. 90, pp. 6143-6147 and Levy et al. (1999) Transgenic Res., Vol. 8, pp. 137-145 in view of Hiendleder et al. (1999) Molec. Reprod. Develop., Vol. 54, pp. 24-31.

Sims teaches the production of calves by nuclear transfer where the donor ICM cell is transferred into a recipient oocyte arrested at MII prior to enucleation (page 6144, col. 1, parag. 1, lines 7-8).

Levy teaches a method of producing homoplasmic mitochondrial hybrid cells or cybrids by enucleating CAP^r 501-1 (HPRT-) cells in the presence of cytochalasin B to produce a cytoplast (page 139, col. 1, parag. 2). Cytochalasin B arrests the ES cells during DNA removal. Levy then electrofuses the enucleated CAP^r cells with AK11.1 ES cells that have been treated with R-6-G, which depletes the cells of functional mitochondria (page 138, col. 2, lines 13-15). The cybrids were cloned in HAT medium (page 139, col. 2, parag. 1). Forty-six out of forty-eight cybrids were homoplastic for the CAP^r mutation (page 143, col. 1, parag. 1, lines 7-8).

Hiendleder teaches calves produced by nuclear transfer exhibit mitochondrial heteroplasmy (page 26, col. 2, parag. 1, lines 1-6). Hiendleder further teaches cytoplasmic genetic effects in important phenotypic traits in dairy and beef cattle linked to mitochondrial DNA polymorphism (page 25,col. 1, lines 6-11). Further Hiendleder states heterogenous mitochondrial DNA as a result of nuclear transfer methods affects the development of mouse embryos (page 25, col. 1, lines 11-15). Hiendleder offers motivation in stating the mitochondrial genotype of commercially cloned cattle should be controlled to produce clones with identical nuclear and mitochondrial genomes (page 30, col. 2, parag. 1).

Therefore, at the time of the instant invention, it would have been obvious to the ordinary artisan to adapt the method of Sims with the method of Levy to produce homoplasmic cattle in view of Hiendleder teaching cattle produced by nuclear transfer can be heteroplamsic and that such should be avoided for developmental and health issues. The cited prior art supplies the requisite teachings, suggestions and motivation to combine.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah Crouch, Ph.D. whose telephone number is 571-272-0727. The examiner can normally be reached on M-Fri, 6:00 AM to 3:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Deborah Crouch, Ph.D.
Primary Examiner
Art Unit 1632

April 11, 2007